

REMARKS**1. Specification**

The Examiner has again objected to the disclosure because it contains an embedded hyperlink and/or other form of browser executable code (see page 14, description of Figure 4). The Examiner argues that Applicant failed to address this issue in their previous response. Applicant respectfully disagrees. In their response filed August 5, 2004, Applicant specifically amended the description on page 14 to delete the embedded hyperlinks. Reconsideration and removal of the objection is respectfully requested.

2. Rejections under 35 U.S.C. §112, second paragraph

Claims 1-10 and 14-17 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner notes that the limitation "said nucleotide molecules" in the last line of the claim 1 lacks sufficient antecedent basis as claim 1 only refers to "nucleic acid molecules". Applicant has amended claim 1 by replacing the term "said nucleotide molecule" with "said nucleic acid molecules" to obviate the rejection. Reconsideration and removal of the rejection is respectfully requested.

5. Rejections under 35 U.S.C. §102 and 35 U.S.C. §103

The Examiner has repeated the anticipation and obviousness rejections contained in the prior office action. Claims 1-3, 6-10, 14, 16-17 and 19-20 have been rejected under 35 U.S.C. §102(e) as being anticipated by Ness et al. (U.S. Patent No. 6,613,508 filed on July 22, 1997). The Examiner has also rejected claims 4, 5 and 18 as being unpatentable under 35 U.S.C. §103(a) over Ness in view of Shuber, Cros and/or the Strategene catalog. Finally, the Examiner has rejected claim 15 as being unpatentable over Ness et al. in view of Cook et al. (US Patent

No. 5,614,617). Applicant respectfully traverses both the anticipation and obviousness rejections.

The Examiner argues that Ness anticipates the claimed method as it teaches a method for genotyping a selected organism comprising the steps of (a) combining tagged nucleic acid molecules with a selected target molecule under conditions and for a time sufficient to permit hybridization of the tagged molecules to the target molecule, wherein a tag is correlative with a particular fragment; (b) separating the tagged nucleic acid molecules by sequential length or by size; (c) cleaving the tag from the tagged fragment, and (d) detecting the tag by non-fluorescent spectrometry or potentiometry and therefrom determining the genotype of the organism. The Examiner further argues that the tagged nucleic acid molecules taught by Ness are with different mass and, consequently, Ness discloses hybridization of nucleic acid molecules to a set of probes of different nucleobase sequences, wherein each probe has a mass that differs from one of all the other probes as recited in step (a) of claim 1, the separation of non-hybridized probes and the detachment of the hybridized probes as recited in steps (b) and (c) and the analysis of the probe in step (d) and detecting the nucleotide sequence in the nucleic acid molecules by means of the probes hybridized to the nucleotide sequence as recited in step (e). Accordingly, the Examiner concludes that Ness reads on the pending claims. Applicants respectfully disagree.

As noted in Applicant's prior response, the Ness reference relates to nucleic acid molecules which throughout the process carry tags and wherein the method always comprises the steps of cleaving the tags from the probes and subsequently detecting the tags (see, col. 2, lines 46-47 and 62-63; col. 54, lines 46-47; col. 4, lines 41-47 and col. 6). As noted in the Ness reference, the Ness "probe" is comprised of two components: a tag and a nucleic acid fragment. The tag is defined at col. 15, line 27 et seq. to generally refer to a chemical moiety used to uniquely identify a molecule of interest. These tags are separated from the DNA fragment of the "probe" and subsequently analyzed using e.g. electrospray mass spectrometry. Thus, the Ness method involves separating, cleaving and detecting the "tag" element of the tagged fragment, not the "fragment" itself to deduce the identity of the target sequence. This is diametrically opposed to the instant method wherein the probe (i.e. the nucleic acid fragment itself) is isolated and analyzed.

Simply stated, Ness does not analyze the entire "probe" or nucleic acid fragment of the probe but rather merely isolates the tag and subjects the tag to analysis. Ness, therefore, clearly relates to the detection and analysis of tags as opposed to probes. This is a critical distinction. Unlike the present invention, Ness certainly does not teach or disclose the exclusion or elimination of the step of cleaving the tags from the probes, nor of the complete omission of the tags. From the Examiner's comments, it appears that the Examiner has equated the "tags" of Ness with Applicant's claimed probes. As discussed above, this is clearly not the case. Moreover, it appears that the Examiner recognizes that Ness merely teaches the mass spectrometrical analysis of tags but argues that the Ness method is just "one of [the] ways to analyze nucleic acid probes" and, as such, anticipates the present claims. Applicant strongly disagrees and submits that Ness cannot be held to anticipate the present claims because it simply fails to teach a required element of the claims, namely step (d) wherein the probes are analyzed by means of electrospray mass spectrometry.

It is axiomatic that to anticipate a claim, the prior art reference must teach each and every element of the claim. MPEP 2131. In the present instance, the claimed method relies on the analysis of the nucleic acid molecules (i.e. the probes themselves) by means of electrospray mass spectrometry. As discussed above, Ness merely analyzes the chemical tags attached to the nucleic acid fragment of its probes using electrospray mass spectrometry. While both methods may be used to draw conclusions or to determine the sequence of the target nucleic acid molecule, they are not the same. As such, Ness cannot be held to anticipate the present claims and the Examiner's attempts to expand the teachings of Ness to do so is improper. Reconsideration and removal of the anticipation rejection is respectfully requested.

As noted above, the Examiner has combined the teachings of Ness with various other prior art references to reject claims 4, 5, 15 and 18 as obvious under 35 U.S.C. §103. Applicant has not reproduced the arguments advanced by the Examiner but respectfully traverses the rejection. Applicant believes that the foregoing comments establish the novelty of the present claims over the Ness reference. Applicant submits that the secondary prior art references cited by the Examiner fail to disclose or suggest the element missing from Ness and, as such similarly fail, either singly or in combination, to teach the claimed invention. As such, the obviousness

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rejections must fall. Reconsideration and removal of the obviousness rejections is respectfully requested.

Favorable consideration and early allowance of the claims earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

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